757-Pos
The Role of Surface Physics in Motility
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Nearly all research in motility has focused sole attention to the solid active elements in the cell while regarding the fluid components (the cytoplasmic and myoplasmic fluids) as primarily passive elements in force generation and movement. The release of the products of hydrolysis has a major effect on the surface energy in the fluid boundary making the fluid proteophobic directly producing force and movement of the structure it is interfaced with.
Considering the fluid surface physics elucidates the following:
1. In muscle a change in surface tension at the fluid-filament boundary of only 6 dynes/cm will producing an increase in proteophobicity resulting in a contractile force equal to the maximum that striated muscle can produce.
2. The optimum position for hydrolysis of ATP to most effectively produce the force on a cargo attached to a microtubule at the 12 o'clock position will be shown to be at the 5 or 7 o'clock position.
3. The viral packing motor function is explained by the release of phosphate ions in the hydrolysis of ATP around the DNA outside the capsid. The free surface energy at the fluid-DNA boundary becomes elevated by the ions which forces the DNA inside where the DNA-DNA interface (as it folds) is less.

758-Pos
Mathematical Model of Multiple Myosin System with Measurement Probes, Focusing on Energy Efficiency
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Myosin is a molecular motor, which slides along actin filaments during ATP hydrolysis. Experimental results of single and multiple molecule measurements show that myosin can slide 15 - 200 nm, which is much lager than molecular size of myosin. To understand sliding mechanism of myosin system, we have developed the model of multiple myosin system with modifying potential function, and analyzed structure of the model. Our results suggest that energy consumption per unit step would be lower by connecting myosins, which is consistent with larger interaction length (IL) experimentally estimated previously (60 - 200 nm, with surface assay). In this study, we will show characteristic structure of potential function of the model to satisfy IL of single and multiple myosin system.
Additionally, in order to verify the model with experimental data, here, we construct model including characteristics of measurement probes (ex. scanning probe (SP), optical tweezers (OT)), and simulate movement of myosin system attached to measurement probes (SP or OT). In order to take into account effects of measurement probes, we construct model of myosin system attached to probes via spring, and simulate movement of myosin system along periodic potential with Langevin equation method. We test effects of spring constant and size of probes. As a result, sliding velocity with SP becomes slower than that with OT, then displacement generating process clearly observed with SP. We will show and discuss our model and experimental data at the meeting.

759-Pos
Actomyosin ADP-States, Non-Hyperbolic Force-Velocity Relation and Processivity of Myosin II in Fast Skeletal Muscle
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The force-velocity relation of striated muscle is incompletely understood with respect to the molecular basis for the maximum shortening velocity and for the non-hyperbolic shape at high forces (low velocities). These, and related issues, are here elucidated using a four-state actomyosin cross-bridge model. Exploration of the parameter space of the model suggests that an actomyosin-ADP state (AM*ADP) with a closed nucleotide pocket, or rather the strain-dependent transition out of this state, has a pivotal role in influencing both the maximum shortening velocity and the shape of the force-velocity relation in the high-force region. Another model property that influences the shape of the high-force region is the detailed dependence of cross-bridge attachment rate on cross-bridge strain. Here, the modelling results argue against ideas of high attachment rate for highly strained cross-bridges. Finally, evidence is presented that actin attached myosin heads (in the AM*ADP state) have the appropriate structural and kinetic properties to position the partner head for rapid attachment to the next site along the actin filament. This would be reminiscent of the role of the corresponding state of myosin V and could form the basis for limited processivity of muscle myosin II to increase the power output during shortening against intermediate loads.

760-Pos
Interactions Between Connected Half-Sarcomeres Produce Emergent Mechanical Behavior in a Mathematical Model of Muscle
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Most reductionist theories of muscle attribute a fiber's mechanical properties to the scaled behavior of a single half-sarcomere. Mathematical models of this type can explain many of the known mechanical properties of muscle but have to incorporate a passive mechanical component that becomes ~300% stiffer in activating conditions to reproduce the force response elicited by stretching a fast mammalian muscle fiber. The available experimental data suggests that titin filaments, which are the mostly likely source of the passive component, become at most ~30% stiffer in saturating Ca2+ solutions. The work described in this manuscript used computer modeling to test an alternative systems theory that attributes the stretch response of a mammalian fiber to the composite behavior of a collection of half-sarcomeres. The principal finding was that the stretch response of a chemically permeabilized rabbit psoas fiber could be reproduced with a framework consisting of 300 half-sarcomeres arranged in 6 parallel myofibrils without requiring titin filaments to stiffen in activating solutions. Ablation of inter-myofibrillar links in the computer simulations lowered isometric force values and lowered energy absorption during a stretch. This computed behavior mimics effects previously observed in experiments using muscles from desmin-deficient mice in which the connections between Z-disks in adjacent myofibrils are presumably compromised. The current simulations suggest that muscle fibers exhibit emergent properties that reflect interactions between half-sarcomeres and are not properties of a single half-sarcomere in isolation. It is therefore likely that full quantitative understanding of a fiber's mechanical properties requires detailed analysis of a complete fiber system and cannot be achieved by focusing solely on the properties of a single half-sarcomere.

761-Pos
Micro-Mechanical Model of Muscle Contraction
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A new mathematical model of skeletal muscle contraction based on two recent single myosin molecule experiments is proposed. First, a single head of Myosin II attached to a large microneedle in the presence of an actin filament shows several 5.5 nm steps in one preferred direction per ATP cycle [1]. Second, a single head of Myosin VI is attached to a bead, trapped in a laser, in the presence of an actin filament and rapid (76 microseconds) and large (250 nm) displacements are imposed to the bead, revealing that the probability for the actin-myosin complex to switch from a weakly attached state to a strongly attached state increases when the scan is performed in the opposite direction of the natural movement of the head itself [2]. We refer to this effect as Strain Sensor (SS). The behavior of the muscle, at the fiber length scale, is interpreted on these new experimental evidences, at the molecular motor scale, allowing the definition of a micro-mechanical model of the contraction. The stepping behavior is modeled with a diffusive process in a well defined potential, following the theory of the Brownian ratchets, while the SS affects the jump process between the attached and the detached state of the myosin head. The model is able to reproduce globally the behavior of the muscle, in its short time scale, related to the power stroke, and in its long time scale, related to the actin-myosin cycle. The response of the model is analyzed by a stochastic simulation of the Langevin equations associated to a population of parallel distributed myosin heads.
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Muscle Regulation I

762-Pos
Comparison of the Binding of the Switch Regions of Cardiac Troponin-I and Skeletal Troponin-I to the Functional N-Domain of Human Cardiac Troponin-C
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In the heart, there are two isoforms of troponin-I (TnI) that are developmentally regulated. The slow skeletal TnI (ssTnI) is the sole isoform expressed in the embryonic or neonatal heart, while cardiac TnI (cTnI) is expressed exclusively in the adult heart. One important distinction between ssTnI and cTnI relates to differences in myofilament Ca^{2+}-sensitivity of force development under acidic pH conditions. Hearts expressing ssTnI show heightened Ca^{2+}-sensitivity compared with hearts expressing cTnI under basal conditions. This isoform-specific